Poets Knew It All Along

Science Finally Finds Out That Girls Are Chimerical; You Know, Xn/Xa

By Joshua Lederberg

THE CHIMERICAL nature of woman has been a preoccupation of poets since the dawn of literature. Recent biological research has given unexpected scientific weight to this concept of femininity. As usual, the fabric of new insight is woven from surprising threads—research in blood poisons, the eating of fava beans in Italy and Greece, the mottling of fur coloration in mice, colorblindness and the biochemistry of hereditary bleeders (hemophilia).

Science and Man

In English, man, the species, is confused with man, the sex. So we follow Bernstein rather than Follett among the stylists and say humans for men plus women.

As every human should know, sex is determined by a special pair of chromosomes —XX for women and XY for men—one of 23 pairs in normal humans. All the eggs produced by a woman normally contain a single X. Half the sperm of a man carry one X and half carry a Y. The sex of an offspring is determined at the time of conception, depending on which has fertilized the egg to give either an XX "zygote," female, or an XY, male.

The Y chromosome has no important function other than sex-determination. Man's X carries a packet of genetic information needed for normal development of a number of functions. Some functions have no obvious fundamental connection with sex, but when abnormally developed, different ones can lead to such diseases as colorblindness, hemophilia or sensitivity to fava beans or aromatic chemicals.

These X-linked hereditary diseases are, however, much more frequent in men than women and show a characteristic pattern. The affected male can transmit his altered X only to his daughters; transmitting a Y makes a son. These daughters will not usually show the disease.

If we think of Xn to mean normal and Xa abnormal, the daughters will be Xn/Xa. Then half of *their* sons will be normal, Xn/Y, and half Xa/Y, to show the disease.

WHAT ABOUT the Xn/Xa girls? At first sight, they show a normal appearance. One dose of a normal chromosome usually suffices for nearly normal function in a cell.

For the past five years, however, two women geneticists, Dr. Liane B. Russell of the AEC's Oak Ridge National Laboratories, and Dr. Mary F. Lyon of the Radiobiological Research Unit at Harwell, England, have been studying this question. Inbred laboratory mice, the most favorable experimental material, have been examined in large numbers for research on genetic changes resulting from radiation.

The most convenient of gene-controlled characteristics for such genetic studies is coat coloration, with various tints of brown and black.

Most of the genes for coat color are in the other chromosome pairs, the autosomes, but some have been found in the X chromosomes.

Geneticists have reached the startling conclusion in regard to the latter cases, that the female behaves like a mosaic of the contrasting characteristics. The coat tends to be mottled, with some hairs one color and some the other. In developmental terms this means that a given cell may allow either the Xa or the Xn chromosome to act, but not both.

Human cells in tissue culture show a similar effect for the manifestation of an enzyme, glucose-6-phosphate dehydrogenase. When a tissue from an Xa/Xn individual is dissected into individual cells, and tissue-culture progeny grown from these cells, a given cell strain behaves as if it is either Xn or Xa.

A few rare cases of X-linked skin disease in man have also corroborated the mosaic, that is piebald, manifestation of these chromosomes. More commonly, the "heterozygous" (Xn/Xa) mothers of colorblind boys are usually nearly normal in their color vision. However, more careful study often shows that such women have mosaic retinas, i.e. patches with normal vision and patches with colorblind vision.

VERY LITTLE is known of the ultimate cellular chemistry by which one chromosome is durably turned off at an early stage of development. The X chromosomes show a visible correlate: only one of the X chromosomes in a given cell undergoes molecular copying of its DNA at the normal time in cell division.

Some humans show strange aberrations in chromosome composition, like XXX or XXY. In these cases too, only one X functions. But the latter example also complicates the myth that chimerism is femininity. The XXY individual, though by no means normally developed, is an indubitable male because the Y chromosome determines sex.

The main significance of these findings is for basic research in the way genes work and how cellular functions have evolved. If both Xs of the female worked at full efficiency, this would require some special compensating mechanism to match the single X of the male. So only one X of the female is allowed to be active in a given cell.

If we extrapolate from the retina to the brain we might speculate on the deeper significance of the phenomenon. (However, before we think of the anima versus animus of Jungian psychology in chromosome terms, we should remember that a woman's paternal X came in turn from her grandmother.)

On the other hand, a woman who should happen to be carrying X-linked genes for nerve cell defects may indeed be a cerebral mosaic of normal and abnormal cells and in that sense an essentially dual personality.

For many other functions, like the manufacture of blood-clotting proteins, it may be quite immaterial that the tissues are chimerical, since the effective products are mixed in the circulation.